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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/649,399	08/26/2003	Ben-Zion Dolitzky	1662/60903	6089

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 04/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/649,399	DOLITZKY ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-19,30,31 and 33-43* is/are rejected.

7)☒ Claim(s) *20-29 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/24/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 35 is rejected under 35 U.S.C. 102(b) as being anticipated by Harnden 1990, with Harnden 1989 supplemental.

In Harnden 1990, see the preparation in the first full paragraph on page 501. The crystallization is done from water. The claims recite among others, methanol/water. However, no limits are set on the ratio of the two solvents; the claim would read on e.g. one part per billion of methanol in water. However, tiny traces of methanol would be expected to be present, because the starting material was prepared in methanol. Footnote 8 is Harnden 1989, and as seen in the last paragraph of page 1741, the starting material was made in methanol.

The reasoning is unpersuasive. First, the chloroform extraction is of limited significance, since chloroform is miscible with methanol, and hence the chloroform extraction would bring with it some of the methanol. Second, the solvent removals cannot be exhaustive since it is already known that these compounds form solvates with methanol. Claim 35 does not set any minimum amount. Even the most tiny trace is enough to qualify (see SmithKline Beecham Corp. v. Apotex Corp., 74 USPQ2d 1398 (CAFC 2005)), and applicants cannot argue that there was absolutely no methanol left at all.

Claims 1-3, 5-10, 18-19, 31, 37-43 are rejected under 35 U.S.C. 102(b) as being anticipated by with Harnden 1989; US 5017701, US 5066805; US 5138057, US 6846927, 6342603, Freerer, 6437125, and WO 200006573.

In Harnden 1989, note the crystallization of (14) from Ethyl acetate/hexane. In US 5017701, note column 7, line 31, where it is crystallized from hot n-butanol; the same is seen in example II-5 of 6342603. In US 5066805, see Column 3, where the solid appears to be prepared by evaporation from a chloroform/methanol solution. In US 5138057, see Column 8, lines 11-12 and 33, where it was crystallized from Ethyl acetate/diethyl ether and from n-butanol. In 6846927, the product was recrystallized from n-butanol but then reslurried in n-heptane, stirred and filtered, i.e. triturated with n-heptane. In Freerer, the crystallization was done from hot isopropanol; see last example. A similar procedure was done with in example 9 of 6437125. In WO 200006573, see synthesis example 11, which has trituration with diethyl ether. In Brand, see page 5251, with crystallizing from aqueous acetone.

Insofar as Claim 31 is concerned, the references which recited n-butanol anticipate, and provide further evidence that this is Form II, since the same method is used. Insofar as Claim 18 is concerned, the reference which recites diethyl ether trituration anticipates, and provide further evidence that this is Form I, since the same method is used. Insofar as Claim 30 is concerned, the references which recite isopropanol anticipate, and provide further evidence that this is Form I, since the same method is used.

The traverse is unpersuasive. MPEP 2112 states:

"SOMETHING WHICH IS OLD DOES NOT BECOME PATENTABLE UPON THE DISCOVERY OF A NEW PROPERTY

The claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable. In re Best, 562 F.2d 1252, 1254, 195 USPQ 430, 433 (CCPA 1977)."

In this case, the "unknown property" is the particular crystalline form. This is unknown because the reference is silent on this property. MPEP 2112 goes on to state:

"A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection."

Again, the "CHARACTERISTIC" which the prior art is silent on is the crystalline form.

This is not an ordinary inherency situation where it is not explicitly stated what the product actually is. Here the reference explicitly teaches exactly what the compound is. The only difference is a characteristic about which the reference happens to be silent. See also Ex parte Anderson, 21 USPQ 2nd 1241 at 1251, discussion of Rejection E. There, the decision states, "There is ample precedent for shifting the burden to an applicant to reproduce a prior art product whose final structure or properties are, at least, in part determined by the precise process used in its manufacture." (page 1253). The "properties" branch of that statement applies here.

It is well settled that the PTO can require an applicant to establish that a prior art product does not necessarily possess the characteristics of the claimed product when the prior art and claimed products are identical or substantially identical. An applicant's burden under these circumstances was described in *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433-434 (CCPA 1977) as follows:

> Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. . . . Whether the rejection is based on 'inherency' under 35 U.S.C. § 102, or 'prima facie obviousness' under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products (footnote omitted).

Applicants argue that the solvent was different. Thus, for example, Harnden (1989) uses ethyl acetate/hexane, whereas applicants use ethyl acetate alone or ethyl acetate/toluene. First, the examiner must point out that toluene and hexane are rather similar solvents, as both are hydrocarbons. But more importantly, applicants reasoning seems to be that only ethyl acetate alone or ethyl acetate/toluene will produce form I, and that if one does not use ethyl acetate alone or ethyl acetate/toluene, one does not get Form I. Applicants present no evidence that this is actually true. The specification makes no such assertion. The same is true for the assertion that Form II is made from ethanol or n-butanol. Actually, the specification teaches that quite an assortment of other solvents will make these forms, including IPA, THF, methylene dichloride, acetonitrile, diethyl ether/ methylene dichloride, dimethylacetamide, acetone, acetonitrile/toluene, methylene dichloride/toluene and chloroform. Therefore, any reasoning that the method is different and therefore the product is not there is not accepted. Applicants are also sometimes

drawing very fine distinctions. Thus, for example, at one point applicants state that "Trituration is defined as mixing a solid powder with a solvent, and is different from washing a solid collected on a filter paper with a solvent." This hardly seems any difference at all. If the solid collected was a powder --- which is a fairly broad term – then the prior art process falls within "trituration", since "mixing" is certainly broad enough to cover washing.

If this reasoning were accepted, applicants could patent an old compound simply by making it in a new manner and supplying some characteristic that the prior art didn't happen to mention, such as density (e.g. "density is not 1.4"), melting point, "refractive index of 2.0", solubility in some obscure solvent, spectroscopic data, and then simply point to the silence of the reference, as applicants have done here. Or one could add properties like or "does not explode on tapping" or "in the form of microneedles" or, as here, give the XRD data. It is always possible to add some such property, so this amounts to saying that an old compound can be patented just by making it in a slightly different manner. There is no support for this in law.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 5 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The intention of claim 5 is unclear. The claim limitation in the claim now is already required by claim 1, according to the new claim limitation.

Claims 11-17, 33-34, 36, 41-43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

According to the specification, the methanol solvate and the ethanol solvate both have the XRD pattern as given in claim 11. However, the claim is broader than that. It reads on any solvate which has this XRD pattern. The specification, however, does not disclose that applicants have made any solvate with this which has this XRD pattern, only the methanol and ethanol solvates which have this XRD pattern. This problem can be fixed by inserting the "methanol or ethanol" limitation into the claim.

Claims 30 and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 30 and 35 contradict each other. According to claim 30, if one uses acetonitrile, acetone and other solvents, one gets Form I. According to claim 35, the exact same process gives the monohydrate. The only way to avoid this is to use isopropanol,

which according to the specification example 11 does give a mixture. The problem is that Table 1, runs 9-12 all show that the use of IPA does not give the hydrate at all, but gives just I, mixed with II. Moreover, other solvents such as acetone also fail to give the monohydrate. Applicants need to clarify what produces one and what produces the other, and write the claims accordingly. It is not at all clear that the specification teaches how to make the monohydrate in such a range of solvents, and it is also unclear when IPA gives the monohydrate. Clarification in claim language is required.

The traverse is unpersuasive. Applicants state that "the organic solvents can produce the famciclovir monohydrate by containing low levels of water." But while some solvents specify some water as being present, the first five do not. Applicants cannot point to "low levels of water" when such is not actually required by the claim.

Beyond that, the response does not come to terms with the rejection. According to claim 30, the use of e.g. ethylacetate produces form I. According to claim 35, the exact same process produces the hydrate. This could only be possible if the process produces a mixture, but the specification makes no mention of producing any mixtures of hydrate with something else, except with IPA.

Claim 35 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for DMF/water, does not reasonably provide enablement for all other choices. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The use of non-aqueous solvents makes so sense at all. One cannot make the hydrate without a source of water. Thus, the use of e.g. THF is impossible. Second, Brand

teaches that the use of aqueous acetone gives famciclovir, not famciclovir hydrate. This then casts doubt on other aqueous solvents except for the aqueous DMF in the example.

The traverse is unpersuasive. First, applicants have not dealt with the Brand reference. If aqueous acetone gives famciclovir, not famciclovir hydrate, it is not seen how acetone itself would give famciclovir hydrate. This is the specific reason for the doubts. No claims are anticipated over Brand. It is cited to show that aqueous acetone is taught to make the non-hydrate.

Applicants point to example 11, where the hydrate was formed from IPA. The examiner can only conclude that the IPA was wet. The examiner notes that in example 1, runs 9-12, IPA was used and the hydrtate is not reported as having been prepared. As to water coming from "the moisture in the air", again, why didn't that happen in example 1? Further, the claim does not require that the reaction be run in moist air in circumstances where the solvents do not themselves have water.

Claim Objections

Claims 20-29, 32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed

until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Berch
Primary Examiner
Art Unit 1624

4/12/06